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INVITED REVIEWS AND SYNTHESES

Drivers of population genetic differentiation in the wild: isolation by dispersal limitation, isolation by adaptation and isolation by colonization

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Abstract

Empirical population genetic studies have been dominated by a neutralist view, according to which gene flow and drift are the main forces driving population genetic structure in nature. The neutralist view in essence describes a process of isolation by dispersal limitation (IBDL) that generally leads to a pattern of isolation by distance (IBD). Recently, however, conceptual frameworks have been put forward that view local genetic adaptation as an important driver of population genetic structure. Isolation by adaptation (IBA) and monopolization (M) posit that gene flow among natural populations is reduced as a consequence of local genetic adaptation. IBA stresses that effective gene flow is reduced among habitats that show dissimilar ecological characteristics, leading to a pattern of isolation by environment. In monopolization, local genetic adaptation of initial colonizing genotypes results in a reduction in gene flow that fosters the persistence of founder effects. Here, we relate these different processes driving landscape genetic structure to patterns of IBD and isolation by environment (IBE). We propose a method to detect whether IBDL, IBA and M shape genetic differentiation in natural landscapes by studying patterns of variation at neutral and non-neutral markers as well as at ecologically relevant traits. Finally, we reinterpret a representative number of studies from the recent literature by associating patterns to processes and identify patterns associated with local genetic adaptation to be as common as IBDL in structuring regional genetic variation of populations in the wild. Our results point to the importance of quantifying environmental gradients and incorporating ecology in the analysis of population genetics.

Keywords: isolation by adaptation, isolation by colonization, isolation by distance, isolation by environment, monopolization

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Space, environment and gene flow

The majority of population genetic studies to date focused on the interplay between population divergence through genetic drift and genetic homogenization mediated by gene flow (Wright 1943, 1946; Hutchinson & Templeton 1999; Clegg & Phillimore 2010), which results in a classic pattern of isolation by distance (IBD, Box 1). In the past decades, however, evidence for rapid adaptive trait evolution in the presence of selection has accumulated (reviewed in Hendry & Kinnison 2001; Ellner *et al.* 2011), and the idea that adaptive responses to divergent natural selection may impact genome-wide population structure has gained momentum (Nosil *et al.*

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Box 1
Inferring processes from patterns

IBDL According to Wright (1943, 1946), patterns of isolation by distance (IBD) are determined by an increase in genetic differentiation among populations with increasing geographic distance as a result of reduced gene flow. IBD occurs under a number of assumptions, including populations in gene-flow-drift equilibrium (in which founder effects have been eroded), absence of selection and a reduction in dispersal rates (and gene flow) with increasing geographic distance (Wright 1943, 1946). IBD can occur in subdivided metapopulations, in which populations exchange genes at a rate dependent upon the geographic distance between them, or within a continuously distributed population, in which dispersal of gametes and/or zygotes is spatially restricted (Wright 1946). In order for a pattern of IBD to persist in the landscape, reduced dispersal of individuals has to be maintained in the landscape as compared to free circulation of gametes in a panmictic population. The underlying process of IBD is therefore the process we here name isolation by dispersal limitation (IBDL).

IBA The presence of selection in natural landscapes drives local adaptation in natural populations. As a result of such adaptation, gene flow among ecologically divergent habitats is reduced because of reduced establishment success of immigrants from different environments. The resulting pattern of genetic differentiation is one of isolation by environment (IBE) and generally affects non-neutral variation (both loci under selection and genotypic trait values). When adaptive divergence promotes barriers to gene flow between populations from ecologically divergent habitats, and genetic differentiation at neutral loci increases along with divergence at loci under selection through genome-wide divergence via genetic drift, the underlying process is called IBA (Isolation by Adaptation). For an exhaustive review on the topic, we direct the reader to Nosil *et al.* (2008, 2009).

IBC Patterns generated by colonization history (founder events) are more complex to interpret than the ones generated by IBDL and IBA because they can be determined by several processes, including monopolization and serial colonization. Isolation by colonization (IBC) can be caused by ecological (priority effects) and evolutionary (local adaptation) processes or their interaction. When local adaptation reinforces founder effects that become persistent in the landscape due to a reduction in gene flow among all habitats, IBC leads to a typical monopolization scenario (De Meester *et al.* 2002). In this scenario, founder effects resulting from the numerical advantage (priority effects) of first colonists are reinforced by the reduced establishment success of immigrants that results from rapid genetic adaptation to local conditions by the resident populations. Under monopolization, local genetic adaptation is largely based on standing genetic variation present in the first few colonizers rather than being predominantly fuelled by gene flow, as in IBA. As monopolization tends to freeze founder effects, it results in overall high genetic differentiation among populations and an absence of a relationship between the pattern of neutral genetic differentiation and geographic and ecological gradients (Orsini *et al.* 2013). In case of serial colonization, positive correlations between geographic distance and both neutral and non-neutral genetic variations at loci under divergent selection can be observed, whereas no correlation is expected with traits. Thus, patterns generated by IBC can be confounded with the ones generated by IBDL (Fig. 1).

2009). In particular, two processes have been put forward that emphasize the indirect role of selection in structuring neutral genetic variation within and among natural populations: *isolation by adaptation* (IBA; Nosil *et al.* 2009) and *monopolization* (De Meester *et al.* 2002; Urban & De Meester 2009; Orsini *et al.* 2013; Box 1). Under IBA, divergent selection among populations inhabiting ecologically different habitats creates a barrier to gene flow, thereby promoting divergence via genetic drift (Nosil *et al.* 2009). Under monopolization, local genetic adaptation increasingly reduces effective gene flow among all populations in a given landscape because of a reduced establishment success of immigrants, reinforcing founder events (De Meester *et al.* 2002). Here, we suggest an interpretation of patterns of genetic differentiation along spatial and environmental gradients to assess which processes structure population genetic variation in natural landscapes.

Concepts, terminology and assumptions: IBDL, IBA and IBC

The isolation-by-distance paradigm assumes that genetic differentiation among populations increases with increasing geographic distance as a consequence of dispersal limitation (Wright 1943, 1946; Bohonak 1999). A reduction in dispersal of individuals as compared to a panmictic population leads to a typical pattern of 'isolation by distance' (IBD, Box 1), for which the underlying process is 'Isolation by dispersal limitation' (IBDL). Distinguishing between the process and

the resulting pattern is important because other processes than IBDL can lead to a pattern of IBD, a typical case being, for example, serial colonization (e.g. Ramachandran *et al.* 2005; DeGiorgio *et al.* 2009; Henn *et al.* 2012). IBDL is essentially neutral and does not take into account any change in environmental conditions that may result in differential establishment success of individuals. If effective gene flow does not reflect dispersal of individuals because of reduced establishment success of immigrant genotypes, patterns of IBD should be interpreted with caution as the basic assumptions of the paradigm as put forward by Wright are violated (Bohonak & Jenkins 2003).

When environmental conditions between a source and a receiving habitat differ, a reduced establishment success of immigrants may occur. In this situation, a reduced effective gene flow among habitats may take place as a result of local genetic adaptation, leading either to isolation by adaptation (Nosil & Crespi 2004; Nosil *et al.* 2005, 2008, 2009) or to monopolization (De Meester *et al.* 2002; Urban & De Meester 2009; Orsini *et al.* 2013). At the heart of both processes is the role of selection in driving population genetic structure in natural landscapes as observed at both neutral and non-neutral loci. However, the distribution of genetic variation in the landscape following local adaptation differs between these two processes.

With IBA, a mismatch between genotype and environment results in reduced establishment success of immigrants and thus in reduced gene flow among populations inhabiting ecologically dissimilar habitats (Nosil *et al.* 2008). IBA thus results in a pattern of isolation by environment (IBE, Box 1).

Under monopolization (De Meester *et al.* 2002), local genetic adaptation following colonization results in an enhancement of priority effects through a reduced gene flow among all populations in the landscape (Orsini *et al.* 2013). In its purest form, monopolization assumes that genetic adaptation to local conditions combined with a numerical advantage of the first migrants contributes to a strong priority effect of residents over immigrants. To the extent that the first few founders carry sufficient genetic variation to foster rapid genetic adaptation to the local environment, this may result in a landscape genetic structure that is, to a large extent, dictated by colonization events. Long-lasting founder effects can also be caused by purely ecological priority effects driven by the numerical advantage of the first migrants (Boileau *et al.* 1992). In this case, when populations grow rapidly in size after founding from few individuals, the gene frequency divergence established during colonization is resistant to decay by gene exchange. The advantage of the first migrants is established because they undergo a rapid growth before exchanging migrants, establishing a purely numerical advantage. Genetic differentiation arising during founding can last thousands of generations (as shown in Boileau *et al.* 1992). Persistent long-lasting founder effects are expected to be common in species with large effective population size and with rapid population growth rates, such as aquatic invertebrates and plants. Both ecological and evolution-mediated priority effects result in patterns of landscape genetic structure that are strongly determined by founder effects and thus by colonization history. We hereafter introduce the concept of 'isolation by colonization' (IBC) to describe this pattern (Box 1).

Interpreting patterns in natural landscapes: IBDL, IBA or IBC?

To distinguish among IBDL, IBA and IBC, it is necessary to analyse patterns of correlation of both neutral and non-neutral genetic variations with geographic and ecological distances. Genetic variation is commonly estimated for molecular markers using F_{ST} distances that quantify among-population genetic differentiation relative to the regional genetic variation. Alternatively, genetic variation can be estimated using Q_{ST} values that quantify among-population genetic differentiation relative to the regional genetic variation at genotypic trait values. Geographic distances commonly used are linear Euclidean distances. They can be corrected by information derived from a GIS-based landscape connectivity analysis or transformed for PCNM analysis (Borcard & Legendre 2002; Box 2). Ecological distances reflect differences in environmental variables among habitats. Mantel tests are applied in the study of single environmental gradients, which result in a one-dimensional niche axis (reviewed in Nosil *et al.* 2009). These tests are appropriate when the hypothesis under study can be formulated in terms of distances (Legendre & Fortin 2010). When one tries to grasp the complex nature of natural systems by measuring variation in multiple biotic and abiotic variables interacting at the landscape level, the use of either partial Mantel tests or, preferably, of multivariate ordination analysis is more appropriate (e.g. Manel *et al.* 2010b; Orsini *et al.* 2013). Multivariate analysis is a technique commonly used in community ecology (Beisner *et al.* 2006; Declerck *et al.* 2005, 2011; Legendre & Legendre 2012; Peres-Neto *et al.* 2006) and is more appropriate when multidimensional niches are analysed to identify ecological drivers of population genetic variation (Legendre & Fortin 2010; Orsini *et al.* 2013).

Box 2
Univariate vs. multivariate analysis

Patterns of association between genetic and geographic or between genetic and ecological distances can be tested using univariate or multivariate approaches. Mantel (1967) or partial Mantel tests (Bohonak 2002) are most commonly used in the analysis of linear correlations between environmental gradients and genetic or geographic variation. Traditionally, Mantel tests have been used to test for relationships between genetic data and the spatial layout of the sampled habitats in the landscape (Bohonak 1999, 2002). Recently, with the increasing ecological knowledge of many natural systems, Mantel tests are also applied to study the correlation between ecological and genetic distances. However, these tests are appropriate only when the hypothesis under study can be formulated in terms of distances (Legendre & Fortin 2010). In real landscapes, where multidimensional niche axes are analysed, variation partitioning may be more appropriate to identify ecological drivers of population genetic structure. A multivariate characterization of environmental gradients associated with a variation partitioning analysis following redundancy analysis (RDA) is a more powerful approach (Borcard *et al.* 1992; Peres-Neto *et al.* 2006) if one wants to quantify the relative contribution of environmental and spatial components driving landscape genetic variation. RDA is a multiple linear regression method between a first matrix of dependent and a second matrix of independent (explanatory) variables (Legendre & Legendre 2012). The dependent matrix in landscape genetic analyses is represented by neutral or adaptive genetic variation, or a derived set of principal coordinate variables of pairwise genetic distances (PCoA). The explanatory variables are expressed either as a spatial matrix S (X and Y coordinates or derived distance-based Moran's eigenvector maps, dbMEM), an environmental matrix E (or derived sample loadings following principal component analyses, PCA) or both (Borcard *et al.* 2011; Legendre & Legendre 2012). Variation partitioning following RDA is commonly used to estimate the relative contribution of spatial and environmental variation structuring community composition in a metacommunity context (Borcard *et al.* 1992; Beisner *et al.* 2006; Peres-Neto *et al.* 2006; Declerck *et al.* 2011; De Bie *et al.* 2012), but has recently been applied in a population genetic context (Legendre & Fortin 2010; Vangestel *et al.* 2012; Orsini *et al.* 2013).

Multivariate analysis has major advantages over univariate analysis because (i) it provides a more realistic understanding of complex landscapes, (ii) allows to disentangle the relative contribution of spatial and environmental variation, (iii) allows to account for synergisms among different environmental variables and (iv) reduces type I errors that are commonly associated with multiple univariate testing (Legendre & Fortin 2010; Manel *et al.* 2010a; Orsini *et al.* 2013).

In Fig. 1, predictions for IBDL, IBA and IBC are shown, providing expected patterns of correlations of genetic with geographic and environmental distances for neutral loci, loci under divergent selection and genotypic trait values. In making the predictions outlined in Fig. 1, we assume that ecological and geographic distances are not correlated in the landscape. We are aware that a correlation between geographic and ecological distances may be common in nature. However, in case that these two distances are strongly correlated, the impact of space and environment cannot be easily disentangled and straightforward predictions cannot be made. The correlation between environmental and spatial variables showing more (positive autocorrelation) or less similarity (negative autocorrelation) than expected by random effect is known as spatial dependence (Legendre & Legendre 2012). Studies in landscape genetics adopt different measures to account for spatial dependence (summarized in Manel *et al.* 2010a). One of these approaches is the use of spatial regression methods (Dormann 2009; Manel *et al.* 2010b), including but not limited to Moran's eigenvector maps (Borcard & Legendre 2002; Dray *et al.* 2006; Diniz-Filho *et al.* 2008; Box 3).

The predicted patterns for IBDL are that genetic differentiation at neutral loci increases with increasing geographic distance, as a consequence of reduced gene flow as geographic distances increase (Fig. 1A). The spatial scale at which the correlation between genetic and geographic distance is observed depends on landscape connectivity and dispersal ability of the organism under study. As IBDL is a strictly neutral process, it leads only to predictions for neutral loci. However, when IBDL combines with local genetic adaptation to specific environmental gradients, a positive correlation between variations at loci under divergent selection and ecological distance can be expected (Fig. 1A). Additionally, for loci under selection, a pattern of IBD can be expected when local adaptation is mediated by different alleles across populations (Fig. 1A, dashed lines), whereas a pattern of IBD is probably overruled when the response to selection is mediated by the same allele

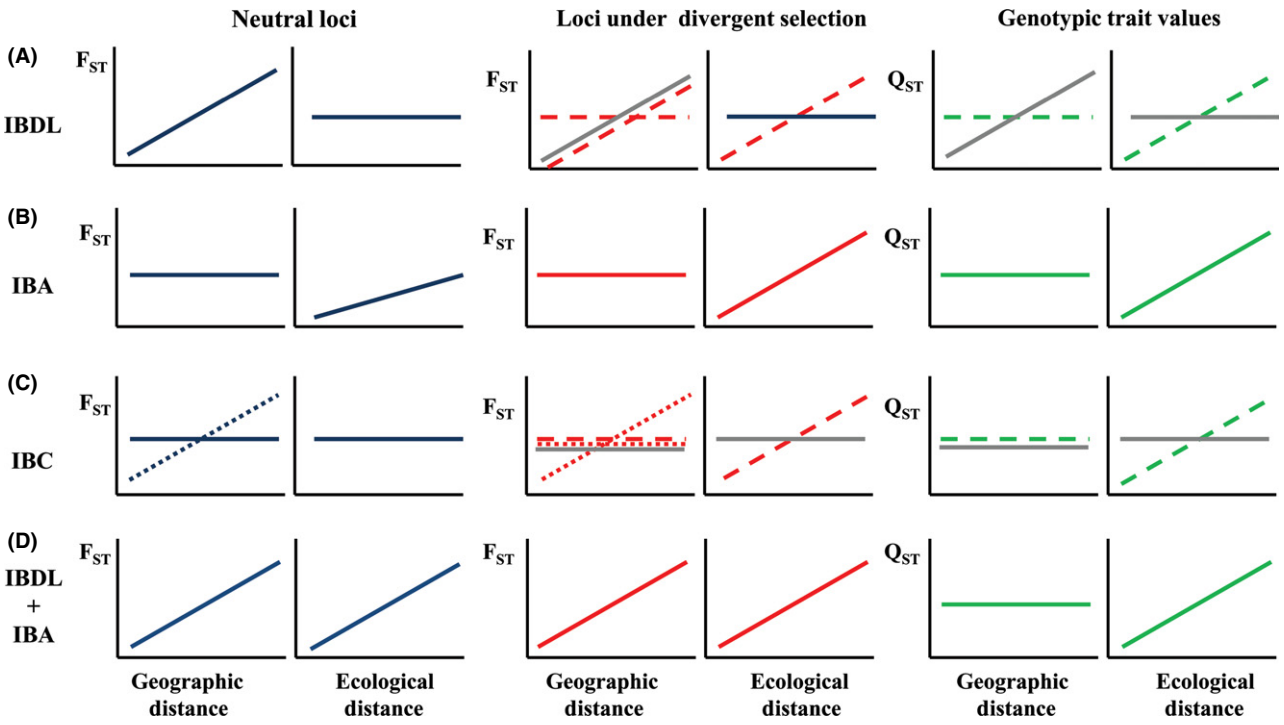

Fig. 1 Predictions for single and combined scenarios. Predicted correlations between genetic differentiation (F_{ST}) and geographic and ecological distances under single and combined scenarios, for neutral loci, loci under divergent selection and genotypic trait values (Q_{ST}, of traits under divergent selection). Pure scenarios are indicated with full lines. Dashed lines in panels A and C indicate the combined effect of the pure scenarios [isolation by dispersal limitation (IBDL) and isolation by colonization (IBC), respectively] with local genetic adaptation. In panel A, the pattern of genetic variation for loci under divergent selection in relation to geographic distance is shown as two alternative scenarios (dashed lines) that reflect the degree to which adaptation to local environmental conditions overrules patterns of isolation by distance (IBD). Dotted lines in panel C indicate IBC caused by serial colonization. In the presence of serial colonization, a correlation of genetic variation for loci under divergent selection and geographic distance can be present or absent depending on the strength of local adaptation (see main text). For completeness, we visualize by grey lines the expectations of loci and genotypic traits not under divergent selection. In panel A, we assume for genes and traits under selection to be a positive correlation with geographic distance caused by IBDL. In panel D, the patterns expected in a combined scenario of IBDL and isolation by adaptation (IBA) are shown.

across populations (Fig. 1A, dashed lines). A pure IBDL scenario makes no predictions concerning the relation between genotypic trait values and geographic nor ecological distance. However, a positive correlation between genotypic trait values for traits under divergent selection and ecological distance can be expected when IBDL combines with local genetic adaptation (Fig. 1A, dashed lines).

Under an IBA scenario, we expect a correlation between genetic distance at loci under selection and ecological distance, as populations are locally adapted and this adaptation is fuelled by gene flow among ecologically similar habitats (Fig. 1B). This gene flow reduces genetic differentiation among populations inhabiting ecologically similar habitats compared to populations inhabiting ecologically dissimilar ones. The association between genetic distance for loci under selection and geographic distance is expected to be weak or absent, as the amount of dispersal is largely determined by ecological distance rather than geographic distance. Under IBA, we expect an association between genetic distances for neutral markers and ecological distance among habitats, although the correlation may be less strong than for loci under divergent selection (see Nosil & Crespi 2004; Nosil *et al.* 2009). The association between neutral genetic variation and ecological distance among habitats is explained by the fact that differential gene flow among ecologically similar and dissimilar habitats also impacts neutral genetic variation (Nosil *et al.* 2008, 2009). As we observe for loci under selection, only a weak or no association is expected between neutral genetic variation among populations and geographic distance among habitats. The predictions for genotypic traits are similar to the ones for loci under divergent selection: a correlation with ecological but not geographic distance (Fig. 1B).

Box 3
Challenges of working with real landscapes

Spatial scale The relative importance of the three processes (IBDL, IBA and IBC) may differ at different spatial scales, with IBDL expected to be more important at larger spatial scales. The spatial scale at which the different processes become important also depends on the dispersal ability of the focal species and the landscape connectivity, two important factors to consider when interpreting the patterns in Fig. 1.

Characterization of environmental gradients Patterns of isolation by environment can be determined by complex interactions among different environmental gradients. It is essential to capture this level of complexity for a correct identification of the forces driving population genetic structure in the wild. This is often not straightforward, and many studies focus on single environmental gradients, which are easier to measure. To analyse the patterns generated by multiple biotic and abiotic factors, often combined with spatial structure, a multivariate analysis may be more appropriate than classic population genetic approaches (see Box 2).

Average levels of genetic variation Single and combined scenarios in Fig. 1 can, in some cases, lead to similar patterns of correlation between genetic variation and geographic and/or ecological distances. In these cases, the average level of genetic differentiation in the landscape may become important to distinguish between patterns generated by single or combined processes. In general, the level of genetic differentiation in the landscape (F_{ST}) is expected to be higher in the presence of combined scenarios.

The relative importance of space and environment Analysing the contribution of space and environment in driving population genetic structure is critical to distinguish among the scenarios discussed in this study. From the literature review, we conducted to screen for the patterns described in Fig. 1, it was evident that studies focusing on neutral genetic variation often did not quantify its association with environmental variation. Conversely, studies focusing on adaptive genetic variation commonly did not asses the role of space on loci under divergent selection. This strongly limits the ability to identify the processes driving population genetic structure in real landscapes. An additional factor complicating the identification of processes driving population genetic variation is the covariation of ecological and spatial gradients, impeding a proper assessment of the independent contribution of either.

Ideally, statistical methods that consider both (i) spatial autocorrelation in allele frequencies generated by gene flow and (ii) spatially structured environmental variables resulting in a spatial structuring of allele frequency distributions should be adopted (Manel *et al.* 2010a,b). Spatial regression methods accounting for spatial dependence between individuals / loci and potentially structuring processes have been put forward. One of the most promising spatial regression approaches is the method of Moran's eigenvector maps (MEM) (Borcard & Legendre 2002; Dray *et al.* 2006; Diniz-Filho *et al.* 2008). MEM analysis produces uncorrelated spatial eigenfunctions used to dissect the spatial patterns of the studied variation (e.g. allele frequencies) into separate scales to be used as predictors in regression (Manel *et al.* 2010a). When spatial autocorrelation and effects of environmental correlates are not constant across the region, regression tree methods can be adopted as an alternative to spatial regression (Dormann *et al.* 2007). These methods are based on an iterative procedure that splits the observations (samples) into a series of two groups in a hierarchical 'tree' (dendrogram-like) structure where the values of the dependent variable are similar within each group based on a specific value of one of the quantitative or qualitative independent values.

A pure ecological IBC scenario is strictly neutral. Therefore, there are no predictions for non-neutral genetic variation (loci and traits under divergent selection) neither in relation to space nor to the environment. Under this scenario, populations are expected to be genetically differentiated at neutral loci, but this differentiation is not expected to correlate with geographic or ecological distance (Fig. 1C). When a purely ecological IBC combines with local genetic adaptation, a positive correlation with ecological distances is expected for loci under divergent selection and for traits (Fig. 1C, dashed lines), whereas predictions remain unchanged for neutral loci as compared to a purely ecological IBC scenario. If local adaption is responsible for a reduction in gene flow among all habitats in the landscape, monopolization occurs (De Meester *et al.* 2002; Orsini *et al.* 2013). This leads to the same predictions as under an IBC scenario combined with local genetic adaptation. However, by explicitly reducing gene flow among all habitats, monopolization is expected to result in a longer-lasting effect of regional genetic differentiation reflecting founder effects. Under monopolization, local genetic adaptation slows the decay of genetic differentiation through time by reducing gene flow. Therefore, monopolization can make the initial founder effects and the resulting pattern of isolation by colonization permanent. If serial colonization occurs (Fig. 1C, dotted lines), neutral loci are expected to have a positive

correlation with geographic distance as a consequence of colonization history. In this scenario, loci under divergent selection can be either correlated or not with geographic distance, depending on the degree to which adaptation to local environmental conditions overrules serial colonization (Fig. 1C, dotted lines). The patterns for genotypic trait values are the same as for IBC combined with local adaptation (Fig. 1C). Overall, under IBC, regional genetic differentiation among populations is expected to be higher on average than under the scenarios of IBD and IBA.

To summarize, processes and patterns illustrated in Fig. 1 can be seen in the light of the interplay between neutral and selective processes and of the role that local adaptation plays, ranging from strictly neutral to non-neutral. For strictly neutral processes, local genetic adaptation only affects genotypic trait values, whereas non-neutral processes drive landscape genetic structure at selected as well as neutral markers through reduced gene flow among populations. IBDL and a purely ecological IBC can be seen as two alternative starting statuses (Fig. 2). When a reduction in gene flow between environments occurs as a result of local adaptation, a process of IBA can be observed (Fig. 2A). Conversely, if local genetic adaptation is fuelled by standing genetic variation present in the founding population that subsequently reduces gene flow among all habitats (even among similar ones, see the case of monopolization), this leads to a strengthening of IBC patterns (Fig. 2A). Whereas IBA results in a detectable change in landscape genetic structure (from Fig. 1A,B), monopolization results in a strengthening of patterns caused by IBC in time and space (Fig. 1C). The link between patterns and processes and how the processes of IBD, IBA and IBC can be linked through local adaptation is depicted in Fig. 2B. The impact of IBDL (reduced gene flow among geographically distant habitats), IBA (reduced gene flow among ecologically dissimilar habitats) and monopolization (reduced gene flow among all habitats in a given region) is shown starting from existing patterns

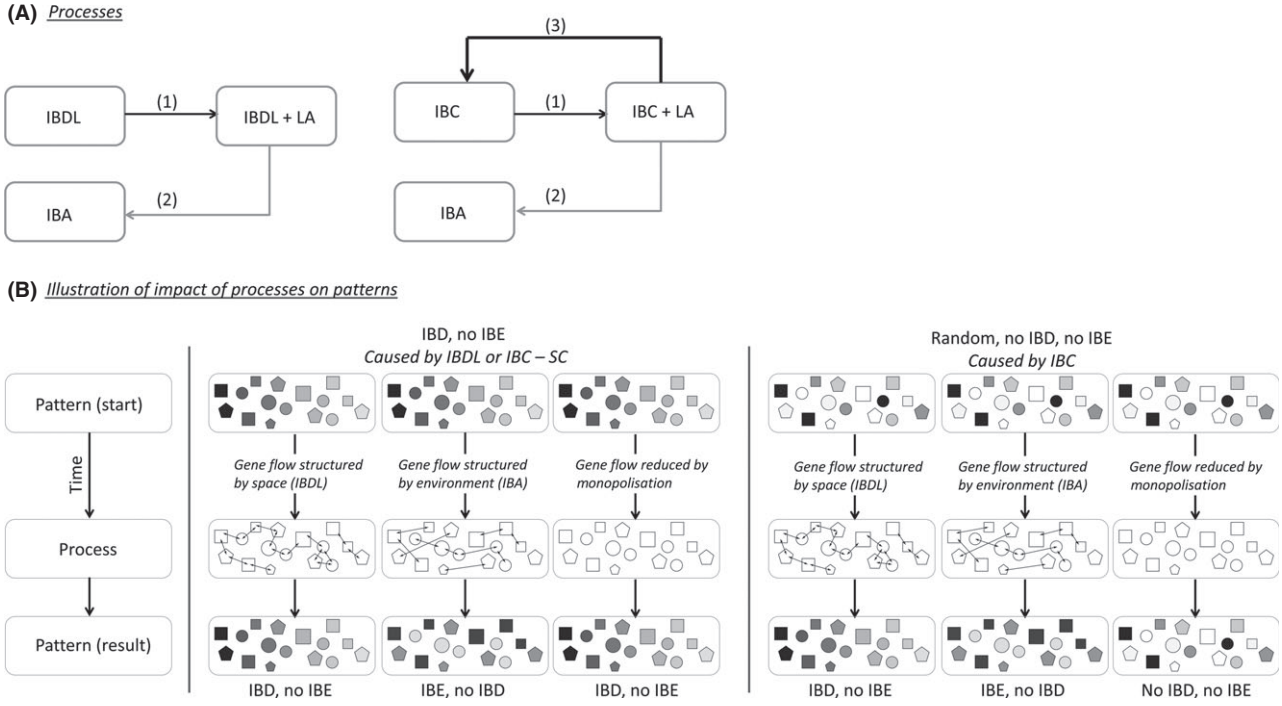

Fig. 2 Linking processes to patterns. Scheme depicting how isolation by distance (IBD), isolation by colonization (IBC) and isolation by adaptation (IBA) can be linked through local adaptation (A) and illustration of the impact of processes on patterns (B). (A) A pattern of IBD [caused by Isolation-by-dispersal-limitation/isolation by dispersal limitation (IBDL)] can be combined with local adaptation (1). If local adaptation leads to a reduced gene flow between environmentally dissimilar patches, this leads to isolation by adaptation (2, IBA; left scheme). Similarly, a pattern caused by isolation by colonization (IBC) can be combined with local adaptation (1). If local adaptation reduces gene flow between environmentally dissimilar patches, this leads to IBA (2). However, if local adaptation is fuelled by standing genetic variation in the founding population and results in a reduction in gene flow among all populations (cf. monopolization), this leads to a reinforcement of the pattern caused by IBC (3). (B) Patterns (upper row of panels) of isolation by distance (IBD) either caused by IBDL or by serial colonization as well as random patterns caused by IBC can evolve into a pattern of IBD, IBE or reinforce IBC (lower row of panels) depending on the processes impacting gene flow: IBDL, IBA or monopolization (middle row of panels). Shapes indicate the environmental characteristics of the habitat (three different environments are shown), and shades of grey indicate neutral genetic similarity between populations in different habitats. Arrows indicate gene flow.

Table 1 Summary of the literature studies

Reference	Study system	Neutral marker (N) F_{ST}	Selected marker (N) F_{ST}	Geographic distance neutral	Ecological distance neutral	Geographic distance selected	Ecological distance selected	Authors' interpretation	Our interpretation based on Fig. 1
Molecular studies									
Plants									
Freeland *et al.* (2010)	*Anthoxanthum odoratum* s (sweet vernal grass)	204AFLP 0.10*	21AFLP	N	Y	N	Y	Different nutrient regimes drive population genetic differentiation-IBA	IBA
Herrera & Bazaga (2008)	*Viola cazorlensis* (hawk moth-pollinated Violet)	332AFLP 0.05	9AFLP 0.40	N	N	—	Y	Differential selection at genome level drives adaptive floral traits divergence	IBC + LA or M
Oetjen & Reusch (2007)	*Zostera marina* (Eelgrass)	20 μsat 0.02*	5μsat —	Y*	Y*	Y	Y	Divergent habitat selection drives population structure	IBDL + IBA
Poncet *et al.* (2010)	*Arabis alpina*	1653AFLP	78AFLP	Y*	N	—	Y	Environmental variation explains genetic variation at candidate loci	IBDL + LA or IBC (serial colonization) + LA
Shi *et al.* (2011)	*Castanopsis eyrei* (subtropical forest tree)	7 μsat 0.03	1 μsat 0.30	Y	Y	Y	Y	Elevation drives population genetic differentiation at neutral and adaptive loci	IBDL + IBA
Vertebrates									
Adnadevic *et al.* (2012)	*Apodemus flavicollis* (yellow-necked mouse)	329AFLP 0.28	142AFLP —	N	N	N	Y	Outlier loci associate with environmental variables which influence population dynamics	IBC + LA or M
Bonin *et al.* (2006)	*Rana temporaria* (common frog)	384AFLP 0.11	8AFLP 0.31	N†	N†	N†	Y†	Outlier loci associate with altitudinal differences	IBC + LA or M
Bourret *et al.* (2013)	*Salmo salar* (salmon)	2939SNP	179SNP	Y	—	Y	Y	Environmental selection drives adaptive divergence	IBDL+ LA or IBDL + IBA or IBC (serial colonization) + LA‡
Campbell & Bernatchez (2004)see also Bernatchez *et al.* (2010)	*Coregonus clupeaformis* (lake whitefish)	392AFLP —	48AFLP —	N§	N§	N§	Y§	Directional selection drives population structure	IBC + LA or M
Deagle *et al.* (2012)	*Gasterosteus aculeatus*	1509SNP 0.19	27SNP 0.11	N	—	N	Y		IBA or IBC + LA or M

Table 1 *Continued*

Reference	Study system	Neutral marker (N) F_{ST}	Selected marker (N) F_{ST}	Geographic distance neutral	Ecological distance neutral	Geographic distance selected	Ecological distance selected	Authors' interpretation	Our interpretation based on Fig. 1
	(threespine stickleback)							Outlier loci linked to stream-lake adaptation identified	
Freedman *et al.* (2010)	*Trachylepis affinis* (African rainforest lizard)	176AFLP —	16AFLP —	Y	Y	Y	Y	Patterns consistent with ecological speciation involving divergent selection identified	IBDL + IBA
Gagnaire *et al.* (2009)	*Anguilla rostrata* (Atlantic eel)	303AFLP 0.001	22AFLP 0.21	Y	Y	—	Y	Natural selection drives population divergence at neutral and selective loci-IBA	IBDL + IBA
Gagnaire *et al.* (2009)	*Anguilla anguilla* (Atlantic eel)	325AFLP 0.0008	9AFLP 0.24	Y	Y	—	Y	Natural selection drives population divergence at neutral and selective loci-IBA	IBDL + IBA
Gomez-Uchida *et al.* (2011)	*Oncorhynchus nerka* (Alaskan sockeye salmon)	41SNP 0.06	4SNP 0.08	Y	Y	Y	Y	Geography and/or ecology influence genetic divergence depending on the spatial scale	IBDL + IBA
Limborg *et al.* (2012)	*Clupea harengus* (Atlantic herring)	265SNP 0.004	16SNP —	Y	N	Y (some loci)	Y	Differential heterogeneous selection explains populations genetic structure	IBDL + LA or IBC (serial colonization) + LA
Nielsen *et al.* (2009)	*Gadus morhua* L. (Atlantic cod)	88SNP 0.04	10SNP —	N¶	Y	N¶	Y	Adaptive population divergence drives population genetic structure and differentiation	IBA
Nunes *et al.* (2011)		318AFLP 0.05	23AFLP 0.24	Y	—	Y	Y		IBDL + LA or IBDL + IBA or IBC

Table 1 *Continued*

Reference	Study system	Neutral marker (N) F_{ST}	Selected marker (N) F_{ST}	Geographic distance neutral	Ecological distance neutral	Geographic distance selected	Ecological distance selected	Authors' interpretation	Our interpretation based on Fig. 1
	Lacerta lepida (ocellated lizards)							Identification of outliers linked to environmental variables	(serial colonization) + LA‡
Invertebrates									
Funk *et al.* (2011)	*Neochlamisus bebbianae* (leaf beetles)	260AFLP 0.06	21AFLP —	N	Y	N	Y	Host-related selection drives population genomic differentiation at neutral and selected loci- IBA	IBA
Manel *et al.* (2009)	*Hylobius abietis L.* (pine weevil)	27AFLP 0.06	9AFLP —	N	Y	—	Y	Abiotic variables are more important than host plant preference in driving population genetic structure	IBA
Nosil *et al.* (2008) see also Nosil *et al.* (2002)	*Timema cristinae* (walking sticks)	456AFLP 0.05	5AFLP 0.22	N‖	Y‖	N‖	Y‖	Host-related adaptation drives population genomic divergence-IBA	IBA
Orsini *et al.* (2012)	*Daphnia magna* (waterflea)	71 µsat 0.12	13 µsat 0.19	N	N	N	Y	Differential selection at genome level-	IBC + LA or M
Orsini *et al.* (2013)		53SNP 0.12	29SNP 0.15	N	N	N	Y	Monopolization	
Scheffer & Hawthorne (2007)	*Phytomyza glabricola* (holly leafminer)	40AFLP 0.04	5AFLP —	Y**	Y	Y**	Y	Host-associated population divergence	IBDL + IBA
Wilding *et al.* (2001) See also Grahame *et al.* (2006)	*Littorina saxatilis* (sea snail)	291AFLP 0.02	15AFLP —	Y	N	—	Y	Divergent selection interests a small proportion of the genome -IBA	IBDL + LA or IBC (serial colonization) + LA
Q_{ST}–F_{ST} studies									
Plants									
				Y	N	N	Y		

Table 1 *Continued*

Reference	Study system	Neutral marker (N) F_{ST}	Selected marker (N) F_{ST}	Geographic distance neutral	Ecological distance neutral	Geographic distance selected	Ecological distance selected	Authors' interpretation	Our interpretation based on Fig. 1
Bekessy *et al.* (2003)	*Araucaria araucana* (puzzle tree)	65RAPD —	2Q_{ST} —					Neutral markers failed to detect divergence in an ecologically important trait	IBDL + LA or IBC (serial colonization) + LA
Jimenez-Ambriz *et al.* (2007)	*Thlaspi caerulescens* (plant)	5 μsat 0.15	4Q_{ST} 0.04	N	N	—	Y	Divergent selection drives patterns of ecotypic variation	IBC + LA or M
Steinger *et al.* (2002)	*Senecio vulgaris* (selfing annual plant)	183AFLP 0.45	6Q_{ST} 0.39	Y	Y	N	Y	Divergent selection contributes to phenotypic differentiation between populations from rural and agricultural habitats	IBDL + IBA
Willi *et al.* (2007)	*Ranunculus reptans* (creeping spearwort)	8allozymes 0.09	8Q_{ST} 0.22	N	Y	—	Y	Genetic drift and selection drive metapopulation structure	IBA
Vertebrates									
Hangartner *et al.* (2012)	*Rana arvalis* (moor frog)	12 μsat 0.03	4Q_{ST} 0.18	Y	Y	N[††]	Y (for some variables)	Divergent selection drives phenotypic divergence among populations along an acidification gradient	IBDL + IBA
Palo *et al.* (2003)	*Rana temporaria* (common frog)	8 μsat 0.23	3Q_{ST} 0.81	Y	Y	N[‡‡]	Y	Directional selection drives phenotypic trait differentiation	IBDL + IBA
Saether *et al.* (2007)	*Gallinago media* (great snipe)	5 μsat 0.03	6Q_{ST} 0.23	Y	Y	—	Y	Technical study on the use F_{ST}–Q_{ST} in conservation	IBDL + IBA
Saint-Laurent *et al.* (2003)	*Osmerus mordax* Mitchill (rainbow smelt)	6 μsat 0.02	5Q_{ST} 0.45	N	Y	N[§§]	Y	Divergent natural selection drives ecotypes structure	IBA
Smith *et al.* (2005)	*Andropadus virens* (little Greenbul, passerine bird)	10 μsat 0.05	5Q_{ST} —	N	Y	N	Y	Natural selection drives populations genetic divergence	IBA
Invertebrates									

Table 1 *Continued*

Reference	Study system	Neutral marker (N) F_{ST}	Selected marker (N) F_{ST}	Geographic distance neutral	Ecological distance neutral	Geographic distance selected	Ecological distance selected	Authors' interpretation	Our interpretation based on Fig. 1
Luttikhuizen *et al.* (2003)	*Macoma balthica* (L.) (bivalve)	mtDNA COI 0.02 5allozymes 0.01	$1Q_{ST}$ 0.42	N	N	—	Y	Habitat divergent selection drives population structure in the presence of gene flow	IBC + LA or M

The studies are divided in two categories: '*molecular studies*', in which variation at neutral loci and loci under selection is measured, and 'Q_{ST}-F_{ST} *studies*', in which variation at neutral molecular markers and genotypic trait values (Q_{ST}) is measured. In each category, plants and animals are listed separately, and animals are divided in vertebrates and invertebrates. The study system including common and scientific name, the number of neutral markers and markers under selection, presence (Y) or absence (N) of correlations of geographic distances and ecological distances with neutral loci and loci under selection or genotypic trait values are listed. The bibliographic reference is also listed with the authors' interpretation in the original publication. F_{ST} values are reported for neutral loci and loci under selection when available. '–' indicates data not available. Our reinterpretation of the patterns observed according to Fig. 1 is listed in parallel to the authors' interpretation. If local adaptation has been detected but no impact on gene flow has been reported (i.e. scenarios as illustrated by dashed lines in Fig 1A, C), we indicate this as 'IBDL + LA' or 'IBC + LA' in the last column of the table. Note that it is impossible to differentiate qualitatively between 'IBC + LA' and monopolization; therefore, we always list both scenarios in the table.

*Neutral loci and loci under selection were analysed together to test for correlation with geographic distance. The values of F_{ST} reported may be inflated and patterns of correlation affected .

†Values not calculated by the authors. They have been extrapolated from the NJ tree constructed for neutral loci and loci under selection, separately [Fig. 4; (Bonin *et al.* 2006)].

‡The two alternative scenarios cannot be distinguished because the relationship between neutral loci and ecological distance was not calculated.

§Values not directly calculated by the authors. They have been extrapolated from the NJ tree constructed for neutral and selected loci separately [Fig. 3; (Campbell & Bernatchez 2004)].

¶The environmental variables analysed vary along a geographic spatial gradient. Therefore, it is not possible to disentangle the effect of geographic structure from the other environmental variables. However, although IBD was not directly calculated, the PCA plot of Fig. 3 (Nielsen *et al.* 2009) does not indicate a clear spatial pattern at neutral markers in the populations analysed.

‖Neither patterns of IBD, nor of IBA were significant when calculated across loci and separately for neutral and selected loci. The patterns were significant when values of F_{ST} at individual loci were regressed against geographic or environmental variation (see (Nosil *et al.* 2009) for details on the analysis).

**The analysis conducted on neutral loci did not differ substantially from the combined analysis including neutral and putatively selected markers.

††Some Q_{ST} show a positive correlation with geographic distance. Variation at these traits, however, is correlated with latitude. Therefore, adaptive variation at these traits and the geographic signal cannot be disentangled.

‡‡Two of the three Q_{ST} analysed in this study do not show correlation with space. However, variation in one of the phenotypic traits covaries with a latitudinal gradient, giving a positive IBD as reported in the original study (Palo *et al.* 2003). Variation in the morphological traits and latitude covaries, therefore, environmental and spatial signal cannot be disentangled.

§§This correlation was not explicitly measured by the authors.

of IBD (caused by IBDL or serial colonization, SC, a special case of IBC) or from random patterns of genetic variation in the landscape caused by IBC (other than serial colonization). A pattern of IBD (left panels, Fig. 2B) remains unchanged if gene flow among habitats in the landscape is structured by space (IBDL) or if gene flow is overall reduced (monopolization). Conversely, if gene flow is structured by the environment (IBA), a pattern of IBD evolves into a pattern of IBE. A random pattern of genetic variation in the landscape (right panels, Fig. 2B) can evolve into a pattern of IBD, IBE or remain unchanged. If gene flow is structured by space, random patterns of genetic variation evolve into a pattern of IBD. If gene flow is structured by local adaptation to environmental conditions, a random pattern evolves into a pattern of IBE. Finally, if gene flow is overall reduced because of local adaptation fuelled by standing genetic variation in the local population (monopolization), the random pattern of genetic variation in the landscape is reinforced.

Combined scenarios

In real landscapes, genetic variation can be structured by a combination of the processes described above. The patterns resulting from combined scenarios involving pairwise combinations of IBDL, IBA and IBC differ from the ones of single scenarios only when IBDL and IBA are combined. The combination of IBC with IBDL and IBC with IBA results in patterns similar to the ones observed for IBDL and IBA, respectively. However, genetic variation at neutral loci is expected to be higher and the patterns weaker in the combined scenarios than in pure scenarios. Patterns generated by the combined impact of IBDL and IBA lead to correlations between neutral and adaptive genetic variations with both geographic and ecological distances for all loci (Fig. 1D). In addition, a correlation between genotypic trait values and ecological distance is expected. Under the assumption of no correlation between ecological and geographic distances, the correlation between genotypic trait values and geographic distance is expected to be absent or weak. The lack of correlation with geographic distance can be stronger for quantitative traits than for loci under selection, because different combinations of loci can lead to the same genotypic trait value. Patterns for other combined scenarios are not shown because the resulting patterns do not differ from the ones of single scenarios, except that they are expected to be weaker.

Literature review

In an effort to establish how often the predicted patterns caused by IBDL, IBA or IBC can be observed in natural landscapes, we reviewed a representative number of studies published in the last decade. We focused on the recent literature (last decade) because most of the older studies are limited to the analysis of neutral variation measured with a handful of markers and often do not report any information on neutral variation in relation to environmental gradients. We searched PubMed (NCBI, http://www.ncbi.nlm.nih.gov/) and Web of Science (WOS, http://sub3.webofknowledge.com/) using single keywords as well as a combination of keywords. Our choice of single keywords was: IBD, IBA and monopolization. We also used the following combinations of keywords: (i) genome scans + selection, (ii) population genomics or ecological genomics + selection, (iii) ecology + genetic divergence and (iv) Q_{ST}–F_{ST}. Searches (1) and (2) allowed to identify studies analysing both neutral and adaptive variations in natural populations. Search (3) aimed at identifying studies in which selection among populations is investigated as the main driver of ecological divergence. Search (4) identified studies with parallel analyses of neutral variation as measured at genetic markers and genotypic trait values. Our aim was to select a representative number of studies that carried out analyses for both neutral loci and loci under selection or ecologically relevant traits and that considered both geographic and environmental gradients. Both aspects (neutral + non-neutral and geographic + ecological gradients) are key to our analysis, and this strongly limited the number of studies that could be reassessed following Fig. 1. We only considered studies dealing with intraspecific variation and did not consider speciation, introgression and hybridization processes. Different measures of correlation between geographic and genetic or ecological and genetic variation were accepted: Mantel test, AMOVA, logistic regression and multivariate analysis. Because of the above criteria, of 194 screened studies (147 studies conducted with genetic markers, referred as molecular studies in the following, and 47 F_{ST}–Q_{ST} studies, Table 1), only 17.5% (23 molecular studies and 11 F_{ST}–Q_{ST} studies) contained enough information so that they could be reinterpreted based on the expectations presented in Fig. 1. Based on patterns of correlation between genetic variation and geographic and environmental variations (see notes to the table highlighting where we needed to derive information indirectly), we identified the most likely process or combination of processes driving population genetic differentiation.

Important aspects stand out from the reinterpretation of published studies in the light of the predicted patterns generated by IBDL, IBA, IBC and their combinations. In all studies retained from our literature search, there is evidence of local genetic adaptation and a positive correlation of loci under divergent selection

or genotypic trait values with ecological distance. Hence, we did not observe patterns driven by strictly neutral processes. This may be caused by the fact that studies including both ecological and geographic gradients explicitly study strong environmental gradients promoting local genetic adaptation. Therefore, we do not exclude that purely neutral scenarios exist. Cases where genetic differentiation at neutral markers is solely associated with geographic distance are rare. Only five of 32 cases could be ascribed to IBDL or serial colonization (IBC, dotted lines in Fig. 1). In all other cases – 27 out of 32 – IBA or IBC (other than serial colonization) plays a role in determining the observed patterns. In eight of these 27 studies, IBA was identified unambiguously as the underlying process; in 11 of the 27 studies, a combination of IBDL and IBA was identified as driver of the observed patterns, whereas in seven of the 27 studies, IBC was the identified underlying process. In the latter studies, IBC (other than serial colonization) can be ascribed either to ecological priority effects or monopolization. Only for one of the studies, we could not unambiguously pinpoint to one process and identified IBA or IBC as possible underlying processes driving the observed patterns. Overall, IBA, either alone or in combination with IBDL, seems to be the most common process driving population genetic differentiation in natural systems, explaining the patterns of genetic variation in not less than 19 (potentially 21) of the 32 studies. The influence of dispersal limitation (IBDL) is suggested in at least 11 and potentially up to 17 studies. IBC plays a role in at least seven and potentially 13 studies. The categories of organisms analysed (plants, vertebrates and invertebrates) showed comparable statistics in terms of importance of IBDL, IBA and IBC based on our reinterpretation of the studies listed in Table 1. In all three categories, IBA explains the largest number of studies (important in >50% of the studies), whereas IBC explains at least 20% (potentially 40%) of them. There is a tendency of lower importance of IBDL in invertebrates (15–30% of the studies) compared to plants and vertebrates (30–55% of the studies). The number of studies that conform to our criteria for analysis is too low to make strong claims, but it is interesting to observe that the three categories show different trends. Combined scenarios explain the patterns observed in 37% of the studies reinterpreted according to Fig. 1. In the majority of these studies, the authors' interpretation ascribed the observed patterns to a single scenario. Our survey suggests that combined scenarios are as likely as single scenarios in explaining patterns observed in the studies analysed. The key message is therefore that there is a need for more studies that simultaneously study patterns in relation to both spatial and environmental gradients, because the majority of studies that only focus on either spatial or environmental gradients are difficult to interpret. Interpretation should be open-minded towards both neutral and selective processes, as well as towards their interaction as evidenced by IBA and monopolization.

Concluding remarks

Patterns of genetic variation in natural landscapes are complex and difficult to predict based on a few generalizing rules. Several aspects can contribute to complicate the interpretation of patterns in nature including, among others, the spatial scale at which the study is conducted, possible interactions among environmental factors, colinearity among environmental factors and geographic variation and other confounding effects (Box 3). Although the scheme presented here does not solve all levels of complexity, we argue that both neutral and non-neutral genetic variations should be measured in relation to both spatial and environmental variations to be able to identify processes underlying observed patterns. Failing to quantify correlations of genetic variation with either space or environment limits our ability to interpret patterns in the wild and may lead to an overestimation of either neutral or adaptive processes driving population genetic differentiation. Studies performing a parallel analysis of neutral and adaptive genetic variation are still surprisingly uncommon in the current literature although higher accessibility of next-generation sequencing technologies allows the study of genome-wide variation also in nonmodel species. Even studies investigating genome-wide variation rarely asses the correlation of both neutral and non-neutral genetic variations with both space and environment. They often asses only the correlation between genetic non-neutral variation and environmental variation or, if they focus on neutral genetic variation, only assess its correlation with space. In both cases, the resulting information is insufficient to identify processes driving genetic variation in the landscape. Our literature survey indicates that only assessing the patterns of correlation between neutral variation and space leads to the correct identification of underlying processes in only 15% of the cases. Similarly, no unequivocal identification of processes can be made when one measures only variation at loci or traits under selection and environmental variation. Thus, we make a strong plea for more studies that account for the role of space as well as environment on both neutral and non-neutral genetic variations, as only this combined analysis allows to disentangle complex processes in natural systems. Based on this integrated approach, we show that dispersal limitation, local adaptation and colonization history are all important factors determining

population genetic structure in natural landscapes, both at neutral and non-neutral genetic variations.

An additional important aspect we want to address is to take an encompassing view in characterizing the environment. Many studies analyse the environment by focusing on single environmental gradients, which result in a one-dimensional niche axis. Whereas this approach can be powerful when one wants to link phenotypic and/or genotypic variation underlying a specific environmental gradient, it is insufficient when one wants to assess the effect of complex environments on genetic variation. A multivariate approach is a powerful method to assess the role of space, environment and their interaction and to analyse in parallel the role of several environmental gradients driving population genetic variation. This approach, now established in community ecology, can be successfully applied in population genetics (as shown in Legendre & Fortin 2010; Manel *et al.* 2010b; Orsini *et al.* 2013). We therefore make a strong plea for an increased integration of ecology and population genetics both conceptually and methodologically.

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References

Adnadevic T, Bugarski-Stanojevic V, Blagojevic J, Stamenkovic G, Vujosevic M (2012) Genetic differentiation in populations of the yellow-necked mouse, *Apodemus flavicollis*, harbouring B chromosomes in different frequencies. *Population Ecology*, **54**, 537–548.

Beisner BE, Peres-Neto PR, Lindstrom ES, Barnett A, Longhi ML (2006) The role of environmental and spatial processes in structuring lake communities from bacteria to fish. *Ecology*, **87**, 2985–2991.

Bekessy SA, Ennos RA, Burgman MA, Newton AC, Ades PK (2003) Neutral DNA markers fail to detect genetic divergence in an ecologically important trait. *Biological Conservation*, **110**, 267–275.

Bernatchez L, Renaut S, Whiteley AR *et al.* (2010) On the origin of species: insights from the ecological genomics of lake whitefish. *Philosophical Transactions of the Royal Society of London. Series B, Biological sciences*, **365**, 1783–1800.

Bohonak AJ (1999) Gene flow, and population structure. *The Quarterly Review of Biology*, **74**, 21–45.

Bohonak AJ (2002) IBD (Isolation By Distance): a program for analyses of isolation by distance. *Journal of Heredity*, **93**, 153–154.

Bohonak AJ, Jenkins DG (2003) Ecological and evolutionary significance of dispersal by freshwater invertebrates. *Ecology Letters*, **6**, 783–796.

Boileau MG, Hebert PDN, Schwartz SS (1992) Non-equilibrium gene frequency divergence: persistent founder effects in natural populations. *Journal of Evolutionary Biology*, **5**, 25–39.

Bonin A, Taberlet P, Miaud C, Pompanon F (2006) Explorative genome scan to detect candidate loci for adaptation along a gradient of altitude in the common frog (*Rana temporaria*). *Molecular Biology and Evolution*, **23**, 773–783.

Borcard D, Legendre P (2002) All-scale spatial analysis of ecological data by means of principal coordinates of neighbour matrices. *Ecological Modelling*, **153**, 51–68.

Borcard D, Legendre P, Drapeau P (1992) Partialling out the spatial component of ecological variation. *Ecology Letters*, **73**, 1045–1055.

Borcard D, Gillet F, Legendre P (2011) *Numerical Ecology wit R*. Springer, Dordrecht, London, Heidelberg, New York.

Bourret V, Kent MP, Primmer CR *et al.* (2013) SNP-array reveals genome-wide patterns of geographical and potential adaptive divergence across the natural range of Atlantic salmon (Salmo salar). *Molecular Ecology*, **22**, 532–551.

Campbell D, Bernatchez L (2004) Generic scan using AFLP markers as a means to assess the role of directional selection in the divergence of sympatric whitefish ecotypes. *Molecular Biology and Evolution*, **21**, 945–956.

Clegg SM, Phillimore AB (2010) The influence of gene flow and drift on genetic and phenotypic divergence in two species of Zosterops in Vanuatu. *Philosophical Transactions of the Royal Society of London. Series B, Biological sciences*, **365**, 1077–1092.

De Bie T, De Meester L, Brendonck L *et al.* (2012) Body size and dispersal mode as key traits determining metacommunity structure of aquatic organisms. *Ecology Letters*, **15**, 740–747.

De Meester L, Gomez A, Okamura B, Schwenk K (2002) The monopolization hypothesis and the dispersal-gene flow paradox in aquatic organisms. *Acta Oecologica*, **23**, 121–135.

Deagle BE, Jones FC, Chan YF *et al.* (2012) Population genomics of parallel phenotypic evolution in stickleback across stream-lake ecological transitions. *Proceedings. Biological Sciences*, **279**, 1277–1286.

Declerck S, Vandekerkhove J, Johansson L *et al.* (2005) Multigroup biodiversity in shallow lakes along gradients of phosphorus and water plant cover. *Ecology*, **86**, 1905–1915.

Declerck SAJ, Coronel JS, Legendre P, Brendonck L (2011) Scale dependency of processes structuring metacommunities of cladocerans in temporary pools of High-Andes wetlands. *Ecography*, **34**, 296–305.

DeGiorgio M, Jakobsson M, Rosenberg NA (2009) Out of Africa: modern human origins special feature: explaining worldwide patterns of human genetic variation using a coalescent-based serial founder model of migration outward from Africa. *Proceedings of the National Academy of Sciences, USA*, **106**, 16057–16062.

Diniz-Filho JAF, Telles MPC, Bonatto S *et al.* (2008) Mapping the evolutionary twilight zone: molecular markers, populations and geography. *Journal of Biogeography*, **35**, 753–763.

Dormann CF (2009) Response to Comment on "Methods to account for spatial autocorrelation in the analysis of species distributional data: a review". *Ecography*, **32**, 379–381.

Dormann CF, McPherson JM, Araujo MB *et al.* (2007) Methods to account for spatial autocorrelation in the analysis of species distributional data: a review. *Ecography*, **30**, 609–628.

Dray S, Legendre P, Peres-Neto PR (2006) Spatial modelling: a comprehensive framework for principal coordinate analysis of neighbour matrices (PCNM). *Ecological Modelling*, **196**, 483–493.

Ellner SP, Geber MA, Hairston NG (2011) Does rapid evolution matter? Measuring the rate of contemporary evolution and its impacts on ecological dynamics. *Ecology Letters*, **14**, 603–614.

Freedman AH, Thomassen HA, Buermann W, Smith TB (2010) Genomic signals of diversification along ecological gradients in a tropical lizard. *Molecular Ecology*, **19**, 3773–3788.

Freeland JR, Biss P, Conrad KF, Silvertown J (2010) Selection pressures have caused genome-wide population differentiation of *Anthoxanthum odoratum* despite the potential for high gene flow. *Journal of Evolutionary Biology*, **23**, 776–782.

Funk DJ, Egan SP, Nosil P (2011) Isolation by adaptation in Neochlamisus leaf beetles: host-related selection promotes neutral genomic divergence. *Molecular Ecology*, **20**, 4671–4682.

Gagnaire PA, Albert V, Jonsson B, Bernatchez L (2009) Natural selection influences AFLP intraspecific genetic variability and introgression patterns in Atlantic eels. *Molecular Ecology*, **18**, 1678–1691.

Gomez-Uchida D, Seeb JE, Smith MJ *et al.* (2011) Single nucleotide polymorphisms unravel hierarchical divergence and signatures of selection among Alaskan sockeye salmon (*Oncorhynchus nerka*) populations. *BMC Evolutionary Biology*, **11**, 48.

Grahame JW, Wilding CS, Butlin RK (2006) Adaptation to a steep environmental gradient and an associated barrier to gene exchange in *Littorina saxatilis*. *Evolution*, **60**, 268–278.

Hangartner S, Laurila A, Rasanen K (2012) Adaptive divergence in moor frog (*Rana arvalis*) populations along an acidification gradient: inferences from Q(st) -F(st) correlations. *Evolution*, **66**, 867–881.

Hendry AP, Kinnison MT (2001) An introduction to microevolution: rate, pattern, process. *Genetica*, **112–113**, 1–8.

Henn BM, Cavalli-Sforza LL, Feldman MW (2012) The great human expansion. *Proceedings of the National Academy of Sciences, USA*, **109**, 17758–17764.

Herrera CM, Bazaga P (2008) Population-genomic approach reveals adaptive floral divergence in discrete populations of a hawk moth-pollinated violet. *Molecular Ecology*, **17**, 5378–5390.

Hutchinson WF, Templeton AR (1999) Correlation of pairwise genetic and geographic distance measures: inferring the relative influences of gene flow and drift on the distribution of genetic variability. *Evolution*, **53**, 1898–1914.

Jimenez-Ambriz G, Petit C, Bourrie I *et al.* (2007) Life history variation in the heavy metal tolerant plant *Thlaspi caerulescens* growing in a network of contaminated and noncontaminated sites in southern France: role of gene flow, selection and phenotypic plasticity. *New Phytologist*, **173**, 199–215.

Legendre P, Fortin MJ (2010) Comparison of the Mantel test and alternative approaches for detecting complex multivariate relationships in the spatial analysis of genetic data. *Molecular Ecology Resources*, **10**, 831–844.

Legendre P, Legendre L (2012) *Numerical Ecology*. Elsevier, Montreal, Quebec.

Limborg MT, Helyar SJ, De Bruyn M *et al.* (2012) Environmental selection on transcriptome-derived SNPs in a high gene flow marine fish, the Atlantic herring (*Clupea harengus*). *Molecular Ecology*, **21**, 3686–3703.

Luttikhuizen PC, Drent J, van Delden W, Piersma T (2003) Spatially structured genetic variation in a broadcast spawning bivalve: quantitative vs. molecular traits. *Journal of Evolutionary Biology*, **16**, 260–272.

Manel S, Conord C, Despres L (2009) Genome scan to assess the respective role of host-plant and environmental constraints on the adaptation of a widespread insect. *BMC Evolutionary Biology*, **9**, 288.

Manel S, Joost S, Epperson BK *et al.* (2010a) Perspectives on the use of landscape genetics to detect genetic adaptive variation in the field. *Molecular Ecology*, **19**, 3760–3772.

Manel S, Poncet BN, Legendre P, Gugerli F, Holderegger R (2010b) Common factors drive adaptive genetic variation at different spatial scales in *Arabis alpina*. *Molecular Ecology*, **19**, 3824–3835.

Mantel N (1967) The detection of disease clustering and a generalized regression approach. *Cancer Research*, **27**, 209–220.

Nielsen EE, Hemmer-Hansen J, Poulsen NA *et al.* (2009) Genomic signatures of local directional selection in a high gene flow marine organism; the Atlantic cod (*Gadus morhua*). *BMC Evolutionary Biology*, **9**, 276.

Nosil P, Crespi BJ (2004) Does gene flow constrain adaptive divergence or vice versa? A test using ecomorphology and sexual isolation in *Timema cristinae* walking-sticks. *Evolution*, **58**, 102–112.

Nosil P, Crespi BJ, Sandoval CP (2002) Host-plant adaptation drives the parallel evolution of reproductive isolation. *Nature*, **417**, 440–443.

Nosil P, Vines TH, Funk DJ (2005) Perspective: reproductive isolation caused by natural selection against immigrants from divergent habitats. *Evolution*, **59**, 705–719.

Nosil P, Egan SP, Funk DJ (2008) Heterogeneous genomic differentiation between walking-stick ecotypes: 'isolation by adaptation' and multiple roles for divergent selection. *Evolution*, **62**, 316–336.

Nosil P, Funk DJ, Ortiz-Barrientos D (2009) Divergent selection and heterogeneous genomic divergence. *Molecular Ecology*, **18**, 375–402.

Nunes VL, Beaumont MA, Butlin RK, Paulo OS (2011) Multiple approaches to detect outliers in a genome scan for selection in ocellated lizards (*Lacerta lepida*) along an environmental gradient. *Molecular Ecology*, **20**, 193–205.

Oetjen K, Reusch TB (2007) Genome scans detect consistent divergent selection among subtidal vs. intertidal populations of the marine angiosperm *Zostera marina*. *Molecular Ecology*, **16**, 5156–5167.

Orsini L, Spanier KI, De Meester L (2012) Genomic signature of natural and anthropogenic stress in wild populations of the waterflea *Daphnia magna*: validation in space, time and experimental evolution. *Molecular Ecology*, **21**, 2160–2175.

Orsini L, Mergeay J, Vanoverbeke J, De Meester L (2013) The role of selection in driving landscape genomic structure of the waterflea *Daphnia magna*. *Molecular Ecology*, **22**, 583–601.

Palo JU, O'Hara RB, Laugen AT *et al.* (2003) Latitudinal divergence of common frog (*Rana temporaria*) life history traits by natural selection: evidence from a comparison of molecular and quantitative genetic data. *Molecular Ecology*, **12**, 1963–1978.

Peres-Neto PR, Legendre P, Dray S, Borcard D (2006) Variation partitioning of species data matrices: estimation and comparison of fractions. *Ecology*, **87**, 2614–2625.

Poncet BN, Herrmann D, Gugerli F *et al.* (2010) Tracking genes of ecological relevance using a genome scan in two independent regional population samples of *Arabis alpina*. *Molecular Ecology*, **19**, 2896–2907.

Ramachandran S, Deshpande O, Roseman CC *et al.* (2005) Support from the relationship of genetic and geographic distance in human populations for a serial founder effect originating in Africa. *Proceedings of the National Academy of Sciences of the, USA*, **102**, 15942–15947.

Saether SA, Fiske P, Kalas JA *et al.* (2007) Inferring local adaptation from QST-FST comparisons: neutral genetic and quantitative trait variation in European populations of great snipe. *Journal of Evolutionary Biology*, **20**, 1563–1576.

Saint-Laurent R, Legault M, Bernatchez L (2003) Divergent selection maintains adaptive differentiation despite high gene flow between sympatric rainbow smelt ecotypes (*Osmerus mordax* Mitchill). *Molecular Ecology*, **12**, 315–330.

Scheffer SJ, Hawthorne DJ (2007) Molecular evidence of host-associated genetic divergence in the holly leafminer *Phytomyza glabricola* (*Diptera: Agromyzidae*): apparent discordance among marker systems. *Molecular Ecology*, **16**, 2627–2637.

Shi MM, Michalski SG, Chen XY, Durka W (2011) Isolation by elevation: genetic structure at neutral and putatively non-neutral loci in a dominant tree of subtropical forests, *Castanopsis eyrei*. *PLoS ONE*, **6**, e21302.

Smith TB, Calsbeek R, Wayne RK *et al.* (2005) Testing alternative mechanisms of evolutionary divergence in an African rain forest passerine bird. *Journal of Evolutionary Biology*, **18**, 257–268.

Steinger T, Haldimann P, Leiss KA, Muller-Scharer H (2002) Does natural selection promote population divergence? A comparative analysis of population structure using amplified fragment length polymorphism markers and quantitative traits. *Molecular Ecology*, **11**, 2583–2590.

Urban MC, De Meester L (2009) Community monopolization: local adaptation enhances priority effects in an evolving meta community. *Proceedings of the Royal Society B*, **276**, 4129–4138.

Vangestel C, Mergeay J, Dawson DA *et al.* (2012) Genetic diversity and population structure in contemporary house sparrow populations along an urbanization gradient. *Heredity (Edinb)*, **109**, 163–172.

Wilding CS, Butlin RK, Grahame JW (2001) Differential gene exchange between parapatric morphs of *Littorina saxatilis* detected using AFLP markers. *Journal of Evolutionary Biology*, **14**, 611–619.

Willi Y, Van Buskirk J, Schmid B, Fischer M (2007) Genetic isolation of fragmented populations is exacerbated by drift and selection. *Journal of Evolutionary Biology*, **20**, 534–542.

Wright S (1943) Isolation by distance. *Genetics*, **28**, 139–156.

Wright S (1946) Isolation by distance under diverse systems of mating. *Genetics*, **31**, 39–59.

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